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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/643,755	08/23/2000	Gijs van Rooijen	9369-153/MG	1008

1059 7590 12/16/2003

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EXAMINER	
HELMER, GEORGIA L	

ART UNIT	PAPER NUMBER
1638	22

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/643,755	VAN ROOIJEN ET AL.	
	Examiner	Art Unit	
	Georgia L. Helmer	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3 and 5-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

REQUEST FOR CONTINUED EXAMINATION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 July 2003 has been entered.

2. Claims 1,3, and 5-23 are pending, and are examined in this Office Action. No claims have been amended.

Claim Rejections - 35 USC § 102

3. Claims 1, 3, 5-7, 11, and 13-19 remain rejected under 35 USC 102(b) as being anticipated by Willmitzer et. al. (WO 92/01042), for reasons of record, which are reiterated below:

Willmitzer teaches a method for the production of chymosin in a plant seed comprising introducing into tobacco and potato plant cells a chimeric nucleic acid sequence comprising a seed-specific phaseolin promoter, a nucleic acid sequence encoding pro-peptide chymosin, and a terminator, then growing the plant until it sets

seeds and obtaining chymosin-containing seeds (Abstract, p 4, 5, 10 and 13). Seeds obtained from the transgenic plants are tested to assure that the gene of interest is present. The expressed enzyme can be isolated from the seed (p 3). Willmitzer further teaches including a plant signal sequence (p 5). The pro-chymosin of Willmitzer appears to a mammalian chymosin obtainable from a bovine, sheep, or goat source (p13), since these are the only know nature sources of chymosin (specification, p.1). Since the method of Willmitzer is the same as Applicant's method, and teach the same promoter as preferred by Applicant, the percentage yields would have been an inherent property of the DNA construct used. If Applicant's percentage yields are different from that of Willmitzer, it is suggested that Applicant amend the claims and include specific structures such which would account for this difference. Willmitzer further teaches a method of isolating chymosin by crushing (p 12, line10) plant tissue, fractionating the resulting product (p 12, lines 9-15), contacting this product with a protein binding resin (p 12, lines 20-25). Accordingly Willmitzer anticipates the claimed invention.

Applicant claims are drawn to a method of producing chymosin in a plant seed comprising introducing into a plant cell a chimeric nucleic acid sequence molecule comprising in the 5'-3' direction of transcription: a seed-specific promoter capable of regulating transcript in said plant cell operatively linked to a second nucleic acid sequence encoding a chymosin polypeptide operatively linked to a third nucleic acid sequence capable of terminating transcription in said cell; growing said plant cell into a mature plant capable of setting seed wherein said seed contains chymosin, and

obtaining seed from the mature plant wherein the seed contains at least 0.5% (w/w) chymosin.

Applicant's method steps are identical to those of Willmitzer. Since Applicant method steps are identical to those of Willmitzer, and they teach the same promoter as preferred by Applicant, the percentage yield would have been an inherent property of the DNA construct used. If Applicant's percentage yields are different from that of Willmitzer, Applicant must have done something to make the yields different. It is suggested that Applicant amend the claims and include specifics which would account for this difference.

Applicant traverses, stating primarily that Examiner has no provided any extrinsic evidence establishing that Willmitzer inherently discloses a yield of chymosin of 0.5% of total seed protein. And that therefore, in accordance with the state of the law, Willmitzer cannot be said to anticipate the claims.

Applicant's traversal has been considered and is unpersuasive because the Crown Operations case cited by Applicant deals with product claims whereby the product may not be identical, whereas *the claims of the instant case are drawn to methods. The steps of Applicant's method claims are identical to Willmitzer's.* Applicant failed to show why the method steps of Willmitzer are different from that of Applicants. Since the method steps of Willmitzer are the same as the steps recited in the claims, the end result must be necessity be the same. That is, since the claimed method steps are

taught by Willmitzer, the amount of chymosin expressed by Willmitzer must by necessity be "at least 0.5%".

Applicant traverses, stating primarily that the only enabling disclosure Willmitzer gives with respect to the production of chymosin is using the 35S CaMV promoter which is a constitutive promoter that results in the expression of chymosin in various parts of the plant, and are not directed to expression to the seed as is claims in the present application. Applicant's traversal has been considered and is unpersuasive because the test for adequacy of a prior art disclosure to anticipate or render claims obvious is not the same test as that for adequacy of a patent application disclosure to support claims under 35 USC 112 as taught In re Hafner, 161 USPQ 783, (CCPA 1969).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-8, 10, 11, and 13-23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Willmitzer (WO 92/01042) for reasons of record, as applied to claims 1-7, 11, and 13-19 above, and further in view of Applicants admitted prior art. The teachings of Willmitzer are discussed supra. Examiner's reasons of record are reiterated below:

While Willmitzer teaches the inclusion of a plant signal sequence and terminator in a chimeric construct, Willmitzer does not specifically teach a tobacco PR-S signal sequence and phaseolin terminator. However, the inclusion of a heterologous signal sequence and terminator in a chimeric construct was notoriously well know in the art, as evidenced by the numerous examples set for by Willmitzer (p. 5) as well as by Applicant (p. 9 and 12). Applicant's admitted prior art indicates that a tobacco PR-S signal sequence and phaseolin terminator, as well as their biological properties, were also known at the time the invention was made (p. 9 and 12). Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize any of the known plant signal sequences and terminators of the prior art, including the claimed tobacco PR-S signal sequence and phaseolin terminator, for their know biological properties, in the chimeric construct for expressing the chymosin of Willmitzer without any surprising or unexpected results. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success.

While it is known that seeds can be fractionated into three fractions (oil, aqueous, and insoluble) based on water solubility, Willmitzer does not teach contacting the aqueous fraction with the protein binding resin. However it is well known that proteins are polyelectrolytes, having multiple positive and negative-charged ionic groups. And

that given the phases of oil, water and insoluble, proteins would be found in the aqueous phase. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to take the aqueous phase, for its known biochemical properties, and contact it with the protein binding resin of Willmitzer, to generate the claimed invention, without any surprising or unexpected results.

While Willmitzer teaches methods of protein isolation using a protein binding resin, he does not specifically teach hydrophobic interaction resins. However, it is well known that proteins are amphipathic molecules, having both strongly polar and strongly nonpolar groups. Applicant's admitted prior art indicates that hydrophobic interaction resins and ion-exchange resins were known at the time the invention was made (p. 23, 24, specification). Accordingly it would have been prima facie obvious to one of ordinary skill in the art of the time the invention was made to contact the aqueous fraction, with a hydrophobic interaction resin, for its know biochemical and physical properties, to generate the claimed invention, without any surprising or unexpected results.

While Willmitzer teaches methods of protein isolation using a protein binding resin, he does not specifically teach ion-exchange resins. However it is well known that proteins are polyelectrolytes, having multiple positive and negative-charged ionic groups. Accordingly it would have been prima facie obvious to one of ordinary skill in the art of the time the invention was made to contact the aqueous fraction, with an ion-exchange resin, for its know biochemical and physical properties, to generate the claimed invention, without any surprising or unexpected results.

6. Claims 1-8, and 10-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willmitzer (WO 92/01042) as applied to claims 1-8, 10, 11, and 13-23 above, and further in view of Adang et al (US 5,380,831). While Willmitzer does not teach optimizing the codon usage of the nucleic acid sequence encoding chymosin for use in plants, such practice was well known in the prior art, as evidenced by Adang. Adang teaches expressing a heterologous protein (Bacillus thuringiensis toxin gene) in plants utilizing codons preferred in highly expressed plant proteins. Accordingly, one skilled in the art would have been motivated at the time the invention was made to express a heterologous protein such as chymosin using plant preferred codons for the purpose of optimizing expression of the protein of interest with a reasonable expectation of success

Applicant traverses, stating primarily that the teachings of Adang and Applicant's admitted prior art do not remedy the deficiencies of Willmitzer, mainly because Willmitzer does not anticipate the claimed invention. Applicant's traversal has been considered and is unpersuasive because Willmitzer anticipates the claimed invention, as discussed above.

Remarks

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114, and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after filing of a request of a continued

examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. *Note that Examiner's phone number will change to 571-272-0796 as of 6 January 2004.* The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia L. Helmer PhD
Patent Examiner,
Transgenic Plants-art group 1638
5 December 2003

Phuong Bui 12/14/03
PHUONG T. BUI
PRIMARY EXAMINER